BIOSCIENCES 741 - GENOMICS
FALL SEMESTER, 2021

Dr. Karl J. Fryxell
School of Systems Biology, and the
Interdisciplinary Program in Neurosciences

Contact Information

Course meets: Tuesdays at 4:30 - 7:10 pm, online. Log into the Blackboard course website, click on the "Tools" menu (left panel, below "assessments"), then click on "Blackboard Collaborate Ultra" tool, then click on the "unlocked course room" icon (near the top left of the window).

Office hours: Fridays, 2:00 pm – 4:00 pm online via Zoom:
https://gmu.zoom.us/j/7931936280?pwd=RWV1OC9oVmRpQUNQb3Y5czhURG91UT09#success

E-mail: kfryxell@gmu.edu *(Please use "BIOS 741" as the subject line of your e-mails)*

Telephone: 703-993-1069 *(Calls to my office phone are forwarded via the internet. Please leave a detailed message including your name, class number callback phone number, and dates/times when you are available for me to call you back.*

Course web site: GMU Blackboard web site - includes lecture notes, study questions, and other materials.

Summary: Biology reached a turning point in February, 2001, with the publication of the euchromatic portion of the human genome. Progress since then in genetics, medicine, biotechnology, pharmacology, and many other fields has been increasingly dependent on the data, techniques and concepts of genomics. The basic facts of biology rely upon the molecular anatomy of our chromosomes, just as basic facts of physiology rely upon the anatomy of our nerves and muscles. However, the volume and complexity of genomic sequence data pose significant problems of interpretation, which will occupy biologists for generations to come.

Prerequisites: Graduate standing, plus at least one undergraduate course in genetics and one undergraduate course in molecular biology.

Readings: There is one required textbook for this class: Pevsner (2015) *Bioinformatics and Functional Genomics* (3rd edition, Wiley). The assigned readings from this text are listed below. An additional, introductory text that may be helpful is Gibson and Muse (2009) *A Primer of Genome Science* (3rd edition, Sinauer, Sunderland, MA). Additional readings from the primary research literature will be assigned, and are listed below. These papers are generally available to registered students through the GMU library web site (library.gmu.edu). If not, copies will be posted on Blackboard.

Grading: Grades will be based on midterm (30%) and final (30%) examinations, plus attendance and active participation in class discussions (10%), an abstract of your term paper (5%) and the final draft of your term paper (25%). Midterm and final exams will be short essay, in-class, closed book exams. The midterm exam will cover the first half of the course; the final exam will cover the second half of the course. Midterm and final exams typically consist of about 5 questions, each of which requires an answer about one page in length. These exam questions will focus on the main points in the lectures and assigned readings, as identified by questions at the end of each chapter in the text, and particularly Study Questions that are posted weekly on Blackboard. Students are expected to do the assigned readings before coming to class, and be prepared to participate in class discussions on these subjects. Makeup exams are not given in this course; excused absences from exams require prior permission from the instructor (that means a two-way conversation, not one-way voice mail or e-mail). The use of cell phones (spoken or texting) or internet resources during exams is not allowed.

As topics for term papers, each student will select a paper from the reading list, to be used as an initial focus for their term paper, and then choose a related focus (such as a hypothesis, controversy, or specific subfield) as the scope of their term paper. The abstract (150-300 words) will summarize and justify this specific focus. The final draft of the written term paper will be an expanded, critical discussion of the current scientific state of the art in the area of genomics. Term papers will be typed, double-spaced, including at least 15+ pages of text (plus an additional required title page, plus an additional required abstract page, plus additional required reference pages). Other items may be included (such as illustrations, quotes, acknowledgements, etc) but do not count towards the minimum length of the text. Your paper should cite at least 30 scientific papers (preferably more), all of which are included in your bibliography, and properly cited in your text. Please note that newspapers, internet web sites, course text books, etc. do not count as "scientific papers", and listing a paper in your bibliography without citing it does not count as a "citation". Plagiarism (copying text without proper attribution) is an Honor Code violation and will be prosecuted. However, you may paraphrase text from the scientific literature, provided that you immediately cite your source at the end of that sentence. The final version of your abstract should state your own critical conclusions

[for example, advantages and disadvantages of particular approaches; which results and interpretations are (or are not) well supported; promising directions for the future, etc]. These conclusions should be justified (logically and with supporting evidence) in the text. Term papers and abstracts are due on the dates stated below, with a 10% per day penalty for late papers.

Class Schedule

Week 1 (August 24) Introduction to genomics

Pevsner text: pp. 720-727.

van Nimwegen, E. (2003) Scaling laws in the functional content of genomes. *Trends Genet* 19, 479-484.

Week 2 (August 31) Sequencing methods, BAC fingerprinting, physical maps and FISH

Pevsner text: pp. 377-387; 399-403; 728-737; 966-968.

Lander, E.S. *et al*. (2001) Initial sequencing and analysis of the human genome. *Nature* 409, 860-921 (we will focus this week on pp. 860-875)

Week 3 (September 7) cDNA libraries, EST clusters, gene prediction and functional annotation

Pevsner text: pp. 433-459; 737-745.

Nekrutenko, A. (2004) Reconciling the numbers: ESTs versus protein-coding genes. *Mol Biol Evol* 21, 1278-1282.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. *Nature* 409, 860-921. (we will focus this week on pp. 894-903).

Week 4 (September 14) Bacterial genomes

Pevsner text: pp. 307-309; 797-837.

Dokland, T. (2019) Molecular piracy: redirection of bacteriophage capsid assembly by mobile genetic elements. *Viruses* 11, 1003.

Novick, R. P. and G. Ram (2016) The floating (pathogenicity) island: a genomic dessert. *Trends Genet* 32, 114-126.

Week 5 (September 21) Gene expression analysis

Pevsner text: pp. 460-472; 479-533.

Lenhard, B., et al. (2012) Metazoan promoters: emerging characteristics and insights into transcriptional regulation. *Nat Rev Genet* 13, 233-245.

Merkin, J. et al. (2012) Evolutionary dynamics of gene and isoform regulation in mammalian tissues. *Science* 338, 1593-1599

Week 6 (September 28) Alternative splicing

Barbosa-Morais, N. L. et al. (2012) The evolutionary landscape of alternative splicing in vertebrate species. *Science* 338, 1587-1593.

Kalsotra, A. and Cooper, T. A. (2011) Functional consequences of developmentally regulated alternative splicing. *Nat Rev Genet* 12, 715-729.

Davuluri, R. V. et al. (2008) The functional consequences of alternative promoter use in mammalian genomes. *Trends Genet* 24, 167-177.

Week 7 (October 5) Midterm Examination - covers weeks 1-6 (ABSTRACTS of term papers due today)

Week 8 (October 12) Fall Break - Tuesday classes do not meet this week

Week 9 (October 19) Proteomics

Pevsner text: pp. 539-580.

Vogel, C. and E. M. Marcotte (2012) Insights into the regulation of protein abundance from proteomic and transcriptomic analysis. *Nat Rev Genet* 13, 227-232.

Boellner, S. and K.-F. Becker (2015) Reverse phase protein arrays – quantitative assessment of multiple biomarkers in biopsies for clinical use. *Microarrays* 4, 98-114.

Week 10 (October 26) The eukaryotic chromosome: noncoding and repetitive sequences, chromosome rearrangements and gene families

Pevsner text: pp. pp. 325-365; 957-965; 971-979.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. *Nature* 409, 860-921. (we will focus this week on pp. 879-885; 887-889).

Waterston, R.H., K. Lindblad-Toh, E. Birney et al. (2002) Initial sequencing and comparative analysis of the mouse genome. *Nature* 420, 520-562.

Pehrsson, E. C. et al. (2019) The epigenomic landscape of transposable elements across normal human development and anatomy. *Nat Commun* 10, 5640.

Week 11 (November 2) Genetic polymorphisms, population genetics and human genetics

Pevsner text: pp. 408-410; 986-1004; 1036-1049.

Bentley, D. B. (2003) DNA sequence variation of *Homo sapiens*. *Cold Spring Harbor Symp Quant Biol*. 68, 55-63. (A PDF copy of this article will be posted on the course web site.)

Auton, A. et al. (2015) A global reference for human genetic variation. *Nature* 526, 68-74.

Week 12 (November 9) Class does not meet (Society for Neuroscience meetings)

Week 13 (November 16) The human genome: codon bias, gene density, GC content, recombination, CpG islands

Pevsner text: pp. 806-808; 968-971; 981-986.

Lander, E.S. et al. (2001) Initial sequencing and analysis of the human genome. Nature 409, 860-921. (we will focus this week on pp. 875-879; 885-887; 892-894).

Hinch, A. G. et al. (2011) The landscape of recombination in African Americans. Nature 476, 170-175.

Week 14 (November 23) Epigenetics – DNA methylation

Jones, P. A. (2012) Functions of DNA methylation: islands, start sites, gene bodies and beyond. *Nat Rev Genet* 13, 484-492.

Smith, Z. D. and Meissner, A. (2013) DNA methylation: roles in mammalian development. *Nat Rev Genet* 14, 204-220.

Mellen, M., P. Ayata and N. Heintz (2017) 5-hydroxycytosine accumulation in postmitotic neurons results in functional demethylation of expressed genes. *Proc. Natl. Acad. Sci. USA* 114(37), E7812-E7821.

Week 15 (November 30) Epigenetics - histone modifications.

Term papers due today! Late penalty is 10% per day!

Jin, C. et al. (2009) H3.3/H2A.Z double variant-containing nucleosomes mark 'nucleosome-free regions' of active promoters and other regulatory regions. *Nat Genet* 41, 941-945.

Ernst, J. et al. (2011) Mapping and analysis of chromatin state dynamics in nine human cell types. *Nature* 473, 43-49.

Petty E, Pillus L (2013) Balancing chromatin remodeling and histone modifications in transcription. *Trends Genet* 29, 621-629.

December 14 - Final Exam - 4:30 pm to 7:10 pm. Covers weeks 8-15.